I. A CONSTITUENT OF IRIS ROOT
II. DERIVATIVES OF 8-AMINOQUINOLINE

BY

LESLIE BYRON POLAND
B.Ed., Illinois State Normal University, 1934
M.S., University of Illinois, 1935

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE UNIVERSITY
OF ILLINOIS, 1941

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I. A CONSTITUENT OF IRIS ROOT

INTRODUCTION

Only a few species of iris have been examined for the presence of glycosides. A glucoside of an isoflavone, tectorigenin,[8] has been isolated from the rhizomes of *Iris tectorum Maxim* and of *Belemconda Chinensis (L.) Leman.*

The purpose of the present investigation was to develop a procedure for the extraction of the glycoside from the rhizomes of the common iris, *Iris germanica*, and to determine its compostion.

HISTORICAL AND DISCUSSION OF RESULTS

Twelve compounds occurring as glucosides have been isolated from natural sources for which isoflavone structures have been put forth. They are prunitrin,[1] genistin,[2] sophoricoside,[3] daidzin,[4] ononin,[5] pseudobaptisin,[6] iridin,[7] tectoridin,[8] tatoin,[9] methylgenistein,[9] methylisogenistin,[9] and isogenistin.[9] By studying the properties of the compound isolated from the common iris and identifying its degradation products, it should be possible to determine the composition of the glycoside and to establish its identity or non-identity with the previously described glycosides.

The dried rhizomes were powdered and extracted with alcohol. Tannins were then removed by precipitation with lead acetate and the solution evaported to dryness. The solid was extracted with ethyl acetate and the remaining residue stirred with water. The insoluble glycoside was removed by filtration. In this way there was obtained 1.4 g. of the glycoside from 9.3 kg. of rhizomes. From the filtrates there was obtained 3.2 g. of the aglucone.

The analysis and melting point of the glycoside agreed with those previously reported for iridin. Hydrolysis yielded glucose and the aglucone. Analysis of the latter and its diacetate were quite different from those of irigenin and its acetate. Analysis showed that the new aglucone contained two hydroxyl and two methoxyl groups, whereas irigenin has three of each of these functional groups. The aglucone was degraded by the action of alkali, but no definite crystalline products could be isolated. The analyses suggest the formula $C_{16}H_8O_2(OH)_2(OCH_3)_2$ for the aglucone.

SUMMARY

A procedure has been developed for the isolation of a glucoside and its aglucone from the rhizomes of *Iris germanica*. The sugar component was shown to be glucose. The aglucone was different from previously described substituted isoflavones.

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II. DERIVATIVES OF 8-AMINOQUINOLINE

INTRODUCTION

One of the useful synthetic antimalarial compounds in use today is 6-methoxy-8-(ω-diethylamino-α-methylbutyl)-aminoquinoline, known as plasmoquin. Other similar quinoline derivatives, with a $-NH(CH_2)_nN(C_2H_5)_2$ chain in position 8, also show strong antimalarial action. Another compound which shows considerable antimalarial activity is the aliphatic diamindine, 1, 11-undecanediamidine. It seemed likely, therefore, that the replacement of the terminal diethylamino group in the $-NHCH(CH_3)(CH_2)_nN(C_2H_5)_2$ side chain by an amidine group would result in a compound with antimalarial activity.

Since the amidines can be prepared from the corresponding nitriles, the purpose of the present investigation was to develop a method for the preparation of nitriles of the type 8-(5-capronitrile-amino)-quinoline.

THEORETICAL AND DISCUSSION OF RESULTS

Secondary amines have been prepared from nitro compounds and aldehydes, or from primary amines and aldehydes by reductive alkylation in the presence of Raney nickel.[1,2] This suggested the reaction of 8-nitroquinoline or 8-aminoquinoline and ketonitriles of the general formula $CH_3CO(CH_2)_nCN$ in the presence of hydrogen and Raney nickel as a method for the synthesis of the desired nitriles. The reduction of the anil formed by the reaction of 8-aminoquinoline and a ketonitrile should also produce the substituted nitrile. Secondary amines of 8-aminoquinoline[3] have been prepared by the reaction of 8-aminoquinoline and bromonitriles of the type $Br(CH_2)_3CN$. The reaction of 8-aminoquinoline and bromonitriles of the type $CH_3CHBr(CH_2)_3CN$ should also furnish a method for the synthesis of these nitriles.

The 8-aminoquinoline was prepared by the method of Smith and Getz,[4] and 6-methoxy-8-aminoquinoline was synthesized as follows: *p*-anisidine → *p*-acetanisidine[5] → *o*-nitro-*p*-acetanisidine[6] → *o*-nitro-*p*-anisidine[6] → 6-methoxy-8-nitroquinoline[4] → 6-methoxy-8-aminoquinoline.[4] The over-all yield of 6-methoxy-8-aminoquinoline from *p*-anisidine was approximately 25 per cent.

Attempts to prepare 8-(2-heptylamino)-quinoline by the reductive coupling of 8-nitroquinoline or 8-aminoquinoline and

2-heptanone in the presence of Raney nickel resulted only in the reduction of 8-nitroquinoline to 8-aminoquinoline and 2-heptanone to 2-heptanol. N-(8-Quinolyl)-2-heptanoneimine was prepared by heating a mixture of 8-aminoquinoline and 2-heptanone in the presence of 8-aminoquinoline dihydrochloride, but attempts to reduce it to 8-(2-heptylamino)-quinoline were unsuccessful. Since these methods were not successful with 2-heptanone, they would not be useful with ketonitriles of the form $CH_3CO(CH_2)_nCN$.

Ketonitriles of the type $CH_3CO(CH_2)_nCN$ may be obtained by the reaction of chloroalkyl cyanides with ethyl acetoacetate followed by hydrolysis to the corresponding ketonitrile. This method proved unsuccessful because the reaction between the chloroalkyl cyanide and ethyl acetoacetate took place in very low yields. 4-Ketovaleronitrile [7] was prepared by the addition of liquid hydrogen cyanide to methyl vinyl ketone. 5-Ketocapronitrile was prepared by the following method: γ-acetylpropyl alcohol [8] → γ-acetylpropyl bromide → 5-ketocapronitrile.

An attempt to prepare 5-bromocapronitrile by the following method: 5-ketocapronitrile → 5-hydroxycapronitrile → 5-bromocapronitrile was unsuccessful because reduction of the keto group to the secondary alcohol produced simultaneous reduction of the nitrile group to the amine. 5-Bromocapronitrile was synthesized as follows: γ-acetylpropyl alcohol → 1,4-pentanediol → 1,4-dibromopentane → 5-bromocapronitrile.

8-(5-Capronitrileamino)-quinoline was prepared by the treatment of 8-aminoquinoline with 5-bromocapronitrile in the presence of potassium iodide and anhydrous sodium carbonate. The yield in this reaction was only 5-10 per cent of the theoretical amount under the conditions found for the reaction.

SUMMARY

4-Ketovaleronitrile was prepared by the action of liquid hydrogen cyanide on methyl vinyl ketone in the presence of anhydrous potassium carbonate.

5-Ketocapronitrile was prepared by converting γ-acetylpropyl alcohol into γ-acetylpropyl bromide which was treated with potassium cyanide to give the 5-ketocapronitrile.

6-Methoxy-8-aminoquinoline was synthesized from *p*-anisidine by the following series of reactions: *p*-anisidine → *p*-acetanisdine

→ *o*-nitro-*p*-acetanisidine → *o*-nitro-*p*-anisidine → 6-methoxy-8-nitroquinoline → 6-methoxy-8-aminoquinoline.

N-(8-Quinolyl)-2-heptanoneimine was prepared by heating a mixture of 8-aminoquinoline and 2-heptanone in the presence of a small amount of 8-aminoquinoline dihydrochloride.

5-Bromocapronitrile was synthesized from γ-acetylpropyl alcohol by the following series of reactions: γ-acetylpropyl alcohol → 1,4-pentanediol → 1,4-dibromopentane → 5-bromocapronitrile.

8-(5-Capronitrileamino)-quinoline was prepared by the treatment of 8-aminoquinoline with 5-bromocapronitrile in the presence of potassium iodide and anhydrous sodium carbonate.

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VITA

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